New drug combination delayed disease progression for subgroup of women with metastatic breast cancer

12 December 2013

Adding the drug dasatinib to a standard antihormone therapy, letrozole, doubled the time before disease progressed for women with hormone receptor-positive, HER2-negative metastatic breast cancer, according to results of a phase II clinical trial presented here at the 2013 San Antonio Breast Cancer Symposium, held Dec. 10-14.

Dasatinib is approved by the U.S. Food and Drug Administration for the treatment of chronic myelogenous leukemia. One of the ways it works is by blocking the activity of a protein called Src, which has been recently implicated in the spread of breast cancer to bones.

"Patients with metastatic breast cancer desperately need new treatment options that can lengthen and improve the quality of their lives," said Dev Paul, D.O., Ph.D., breast oncologist at U.S. Oncology and Rocky Mountain Cancer Centers in Denver, Colo. "Because several studies have linked high levels of Src activity to breast cancer metastasis to the bone, we wanted to see whether combining letrozole and dasatinib as first-line treatment for metastatic breast cancer would improve the clinical-benefit rate and progression-free survival compared with letrozole alone.

"We are encouraged to see that the combination doubled progression-free survival time," he added. "But this was a small study, and we really need a biomarker to measure Src activity in breast tumors, so that we can better determine which patients will be most likely to benefit from the addition of dasatinib to letrozole."

Paul and colleagues enrolled 120 postmenopausal women with locally recurrent or metastatic hormone receptor-positive, HER2-negative breast cancer in the phase II clinical trial. They randomly assigned 63 participants to letrozole and 57 to letrozole plus dasatinib. The primary aim of the study was to determine whether adding dasatinib to letrozole increased the clinical-benefit rate. The clinical-benefit rate is the number of patients who had a complete response, plus the number who had a partial response, plus the number who had stable disease for six or more months.

The researchers found that adding dasatinib to letrozole did not increase the clinical-benefit rate compared with letrozole alone. When a second measure of the study's outcome was analyzed, the combination therapy was shown to dramatically improve progression-free survival. Progression-free survival for patients receiving dasatinib and letrozole was 20.1 months compared with 9.9 months for letrozole alone.

Patients receiving dasatinib plus letrozole did experience additional side effects but none were considered severe adverse events, according to Paul, and most patients tolerated the full dose of dasatinib.

"Although these data suggest that adding dasatinib to letrozole improves progression-free survival for postmenopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer, we would like to find a biomarker for Src activity in the breast before conducting larger clinical studies of this drug combination," said Paul.

Provided by American Association for Cancer Research